Essay

Freedom of Speech and the FDA's Regulation of Off-Label Drug Uses

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Introduction

To be approved by the Food and Drug Administration ("FDA"), a prescription drug must pass a series of rigorous clinical trials. The trials test the drug's safety and effectiveness for a specific condition and a defined subset of patients. Once approved by the FDA, however, doctors are free to prescribe that drug to treat different illnesses, different patient groups, or both. This is known as "off-label use" and it is limited only by the profession's standards of responsibility. Far from being insignificant, off-label use accounts for over one-fifth of prescriptions in the United States,[1] with many of these uses having little or no scientific support.

While off-label use itself is a source of controversy, perhaps more controversial is the FDA's decision to virtually prohibit pharmaceutical companies from marketing those uses to health care professionals. Opponents of the prohibition argue that it infringes upon the companies' First Amendment right to free speech. This Essay argues that the FDA's regulations prohibiting pharmaceutical companies from

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1 *See* Michael I. Krauss, *Loosening the FDA's Drug Certification Monopoly: Implications for Tort Law and Consumer Welfare*, 4 GEO. MASON L. REV. 457, 472 (1996).

marketing a drug's off-label uses to healthcare professionals are, apart from being sound public policy, constitutional. The regulations pass the test for commercial speech set forth in *Central Hudson Gas & Electric Corporation v. Public Service Commission*[2] and curb the industry's incentives to operate in a manner contrary to the public interest. The Essay begins with a discussion of the relevant regulatory framework, then proceeds to an overview of the arguments for and against the policy. Part III describes the current legal status of the regulations. Finally, Part IV defends both the constitutionality and desirability of the restrictions.

I. Regulatory Framework

When the FDA grants approval of a drug or medical device, the approval is only for the use applied for and tested.[3] That testing consists of "a rigorous series of pre-clinical and clinical trials" to ensure "that the drug or medical device is both safe and effective for each of its intended uses."[4] In making its decision, the FDA employs the "substantial evidence" standard.[5] As defined in the Federal Food, Drug, and Cosmetic Act,[6] this standard requires that the evidence consist of "adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved" such that it can "fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof."[7]

As the end of the "substantial evidence" definition suggests, a drug's labeling is a key component of the approval process. During the approval process, the FDA "reviews the proposed 'labeling' for the drug, which includes, *inter alia*, all proposed claims about the drug's risks and benefits, as well as adequate directions for use."[8] The FDA only approves a drug "if the labeling conforms with the uses that the FDA has approved."[9] In other words, the labeling cannot include

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2 Cent. Hudson Gas & Elec. Corp. v. Pub. Serv. Comm'n, 447 U.S. 557 (1980).

3 *See* Wash. Legal Found. v. Friedman, 13 F. Supp. 2d 51, 55 (D.D.C. 1998), *vacated sub nom.* Wash. Legal Found. v. Henney, 202 F.3d 331, 337 (D.C. Cir. 2000).

4 *Id.* (citing 21 U.S.C. § 355(a), (b), (j) (2000)).

5 *Id.* (citing 21 U.S.C. § 355(d) (2000)).

6 Federal Food, Drug, and Cosmetic Act, 21 U.S.C. §§ 301–399 (2000).

7 21 U.S.C. § 355(d).

8 *Friedman*, 13 F. Supp. 2d at 55 (citing 21 U.S.C. § 352(f)).

9 *Id.*

any uses that were not tested by "adequate and well-controlled investigations."[10] The goal of this regulation is to ensure that the labels "contain accurate and complete information regarding approved use and risks."[11]

Once the drug is cleared by the government for a specified use, however, nothing prevents health care professionals from prescribing that same drug for entirely different ("off-label") uses.[12] Off-label uses "include treating a condition not indicated on the label, or treating the indicated condition but varying the dosing regimen or the patient population."[13] The practice of off-label prescription is quite common—according to one recent study of 160 commonly prescribed drugs in 2001, off-label prescriptions accounted for twenty-one percent of overall use and nearly fifty percent for cardiac medications and anticonvulsants.[14] Indeed, "off-label use of FDA-approved drugs by physicians is an established aspect of the modern practice of medicine."[15] In fact, physicians may even face malpractice liability for "failing to provide appropriate treatment simply because it is an off-label application."[16] Although the question of whether the FDA could choose to regulate off-label prescriptions is still open,[17] the Supreme Court has looked on the practice approvingly.[18]

Despite the fact that the FDA allows off-label prescription and use, pharmaceutical companies generally may not market those uses to health care professionals.[19] In this case, "marketing" does not simply refer to the magazine and television ads consumers are familiar with.[20] Rather, "[p]romotional activity can include dissemination of

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10 *See* 21 U.S.C. § 355(d).

11 Steven R. Salbu, *Off-Label Use, Prescription, and Marketing of FDA-Approved Drugs: An Assessment of Legislative and Regulatory Policy*, 51 FLA. L. REV. 181, 187 (1999).

12 *See Friedman*, 13 F. Supp. 2d at 55 (citing 59 Fed. Reg. 59,820, 59,821 (Nov. 18, 1994)).

13 *Id*.

14 *Medical Study Results Published by Dartmouth College*, MED. & L. WKLY., June 22, 2007, at 489.

15 *Friedman*, 13 F. Supp. 2d at 56 (citation omitted). "Even the FDA acknowledges that in some specific and narrow areas of medical practice, practitioners consider off-label use to constitute the standard of good medical care." *Id.*

16 Salbu, *supra* note 11, at 190–91.

17 *See Friedman*, 13 F. Supp. 2d at 55–56.

18 *See* Buckman Co. v. Plaintiffs' Legal Comm., 531 U.S. 341, 350 (2001) (noting that "'off-label' usage of medical devices . . . is an accepted and necessary corollary of the FDA's mission to regulate in this area without directly interfering with the practice of medicine").

19 *See Friedman*, 13 F. Supp. 2d at 55.

20 *See* Ralph F. Hall & Elizabeth S. Sobotka, *Inconsistent Government Policies: Why FDA Off-Label Regulation Cannot Survive First Amendment Review Under* Greater New Orleans, 62 FOOD & DRUG L.J. 1, 6 (2007).

scientific information, clinical trial results, and medical articles and textbooks, as well as . . . speeches to physician groups, medical journal distribution and website content."[21] The ban applies to both pharmaceutical companies and their agents, and thus would include physicians who are affiliated with pharmaceutical companies.[22] As critics of the regulation point out, this can result in the same speech, delivered to the same audience by doctors with the same qualifications, being treated differently if one of those speakers has been funded by a pharmaceutical company.[23] The prohibition does not apply, however, to "specific policy needs such as full disclosure to financial investors, clinical researchers and research subjects."[24] Also, health care professionals are free to *request* information concerning off-label uses from the pharmaceutical companies.[25]

II. Justifications for and Criticisms of Off-Label Use, Prescription, and Marketing

Before discussing the merits and constitutionality of off-label marketing, it is useful to examine the arguments for and against off-label processes generally.[26] Given the importance of off-label use to modern medicine, it is not surprising that there are numerous upsides to the practice—primarily its "potential to expedite the development and availability of effective new treatments."[27] The FDA's drug-approval process "commonly take[s] years of time and hundreds of millions of dollars" to navigate.[28] Often, by the time a drug receives FDA approval, physicians and patients often already know about a drug's beneficial off-label uses.[29] This is explained largely by the paucity of research laboratories relative to the number of medical offices pre-

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21 *Id.* (citing 62 Fed. Reg. 64,074, 64,075, 64,076, 64,083 (Dec. 3, 1997)).

22 *See id.* at 8–10.

23 *See id.* at 9–10.

24 *Id.* at 9.

25 *See* Wash. Legal Found. v. Friedman, 13 F. Supp. 2d 51, 58 (D.D.C. 1998), *vacated sub nom.* Wash. Legal Found. v. Henney, 202 F.3d 331, 337 (D.C. Cir. 2000); Hall & Sobotka, *supra* note 20, at 30; Janet Woodcock, A Shift in the Regulatory Approach, Presentation at the FDA Center for Drug Evaluation & Research (July 17, 1997), http://www.fda.gov/cder/present/diamontreal/regappr/sld005.htm.

26 The use of the word "processes" to collectively refer to off-label use, prescription, and marketing is borrowed from Salbu, *supra* note 11, at 192.

27 Salbu, *supra* note 11, at 193.

28 *See* Hall & Sobotka, *supra* note 20, at 7.

29 *Id.*

scribing (and thus testing) off-label uses, as well as the "exacting and laborious methods" of the former.[30]

Not surprisingly, off-label prescription and use also have a significant downside, as the benefits of getting effective drugs to patients more quickly do not come without a cost. One major study concluded that seventy-five percent of all off-label prescriptions "had little or no scientific support," meaning they had not been "proven . . . effective in controlled clinical trials or at least fairly large observational studies."[31] The result is that "[o]pponents of off-label processes converge . . . upon a single basic objection—that the lack of regulatory control over off-label applications endangers human health and human life."[32] In the case of the drug "fen-phen," such fears were realized.[33]

Doctors widely prescribed the FDA-approved fenfluramine (the "fen") in three off-label ways: (1) "use in combination with phentermine" (the "phen"), (2) "the extended use of fenfluramine beyond the brief approved periods," and (3) "the use of fenfluramine by persons overweight but not obese."[34] The FDA later determined that such usage of the drug constituted an "unacceptable risk."[35] The FDA conservatively estimated "that 285,000 fen-phen users suffered damage to heart valves during the brief period in which the combination was widely prescribed."[36]

Just as importantly, "[e]ven in cases in which the off-label use is not 'toxic,' prescribing a drug that is merely not effective may be no less harmful, because the ineffective prescription regimen will have been substituted for an effective one."[37] That off-label use can cause such damage to the public health leads many to the conclusion that the practice is akin to experimenting on the public.[38] It is not surprising, then, that the FDA justifies its prohibition against marketing off-

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30 Salbu, *supra* note 11, at 196–97.

31 Hazel Muir, *Dicing with Death: There's a Good Chance that the Pills Your Doctor Prescribed Will Do You No Good and Might Even Harm You*, NEW SCIENTIST, July 29, 2006, at 38, 40.

32 Salbu, *supra* note 11, at 201.

33 *See id.* at 202–03; *cf.* Wash. Legal Found. v. Friedman, 13 F. Supp. 2d 51, 56–57 (D.D.C. 1998) (discussing the anti-arrythmic drugs encainide and flecainide, whose off-label uses resulted in a 250% increase in mortality, leading to between 3000 and 10,000 patient deaths per year), *vacated sub nom.* Wash. Legal Found. v. Henney, 202 F.3d 331, 337 (D.C. Cir. 2000).

34 Salbu, *supra* note 11, at 203.

35 *Id.* (quoting *FDA Announces Withdrawal of Fenfluramine and Dexfenfluramine*, HHS NEWS, Sept. 15, 1997, at 97–32).

36 *Id.*

37 *Friedman*, 13 F. Supp. 2d at 56–57.

38 *See* Salbu, *supra* note 11, at 204–05.

label uses by arguing that it promotes the public's health and safety.[39] Under that umbrella, the agency has two more specific claims: (1) the policy ensures "that physicians receive accurate and unbiased information so that they may make informed prescription choices," and (2) it provides "manufacturers with ample incentive to get previously unapproved uses on label."[40] At least one court, however, has rejected the former as a legitimate justification.[41]

Contrary to the FDA's position, though, there are also arguments that off-label marketing is a positive practice. First, given the positive effects off-label use *can* have, "off-label marketing may enable the greatest number of potential beneficiaries to receive the treatments best suited to their needs."[42] A prominent example in support of that argument is the acknowledged off-label utility of aspirin in reducing the risk of heart attacks.[43] Despite credible estimates since the 1980s that "publicity for the aspirin treatment could save from 10,000 to 100,000 lives each year," the FDA only recently allowed aspirin manufacturers to make any claims about this benefit of the drug.[44] Given that the off-label use of aspirin was widely known by both physicians and patients, the estimates demonstrate that off-label marketing may be necessary to keep "potentially life-saving" uses from "remain[ing] isolated and limited."[45]

A second rationale for legalizing off-label marketing is that the prohibition may "contribute to sub-optimal patient treatment . . . by cutting off a valuable potential source of cost-containment."[46] With off-label marketing restricted, drug makers are more likely to submit to rigorous FDA-approval procedures, which only one out of 5000 new drugs now completes successfully, at an average manufacturer's cost of $200 million.[47] Those increased research and development costs could translate into increased costs for the public, forcing consumers to pay higher prices "in an environment in which pharmaceutical pricing is already a serious concern."[48] Such an argument

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39 *See Friedman*, 13 F. Supp. 2d at 69.

40 *Id.*

41 *Id.* at 69–70.

42 Salbu, *supra* note 11, at 194.

43 *Id.* at 194–95.

44 Krauss, *supra* note 1, at 471–72.

45 Salbu, *supra* note 11, at 195.

46 *Id.*

47 *See* Krauss, *supra* note 1, at 462.

48 Salbu, *supra* note 11, at 195.

presumes, of course, that the "expense of the tests" will outweigh "the protective functions that they would serve."[49]

A third and final argument for off-label marketing "concerns the resources saved or put to better use by the FDA when off-label applications can be marketed without seeking FDA approval."[50] Money currently spent enforcing the prohibition against off-label marketing could be used to more expediently assess new drugs and devices, allowing drugs to reach patients more quickly.[51] And if the FDA spent fewer tax dollars, the result could be "a reduced public tax burden that would free consumer dollars for spending on pharmaceutical treatments."[52]

III. Current State of the Law

The FDA's prohibition on off-label marketing has resulted in several legal challenges, with opponents claiming that the ban violates the pharmaceutical companies' First Amendment right to free speech.[53] The leading case, from 1998, is *Washington Legal Foundation v. Friedman*.[54] Washington Legal Foundation ("WLF") is a politically conservative non-profit organization dedicated to "shap[ing] public policy and fight[ing] activist lawyers, regulators, and intrusive government agencies at the federal and state levels, in the courts and regulatory agencies across the country."[55] WLF sued on First Amendment grounds to enjoin the FDA from enforcing its prohibition on off-label marketing.[56] The FDA defended by arguing that it was following its mandate to protect the public health and safety, noting that "the ordinary citizen here has little ability to protect himself or herself from the potential harm associated with unproven uses of drugs and devices."[57]

The threshold question for Judge Lamberth was "how to classify the 'speech' at issue."[58] WLF argued that the marketing practices constituted "scientific and academic speech, which is entitled to the highest level of First Amendment protection."[59] The FDA countered with

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49 *Id.* at 195 n.89.

50 *Id.* at 195.

51 *See id.* at 195–96.

52 *Id.* at 196.

53 *See, e.g.*, Wash. Legal Found. v. Friedman, 13 F. Supp. 2d 51 (D.D.C. 1998), *vacated sub nom.* Wash. Legal Found. v. Henney, 202 F.3d 331, 337 (D.C. Cir. 2000).

54 *Friedman*, 13 F. Supp. 2d 51.

55 WLF At-A-Glance, http://www.wlf.org/ataglance.asp (last visited Oct. 19, 2007).

56 *See Friedman*, 13 F. Supp. 2d at 54.

57 *Id.* at 57 (internal quotation omitted).

58 *Id.* at 59.

59 *Id.*

three arguments. First, it maintained that the regulation only prohibited conduct, not speech.[60] Next, it contended that because "the federal government has the broad power to regulate the pharmaceutical industry," the prohibition is only an "incidental encroachment[ ] upon speech.[61] Finally, the Agency argued that the regulation concerned commercial speech, "which is subject to a more relaxed inquiry than core First Amendment speech."[62]

The court quickly dismissed the FDA's first argument, adopting the plaintiff's view that "the activities at issue in this case are only 'conduct' to the extent that moving one's lips is 'conduct,' or to the extent that affixing a stamp and distributing information through the mails is 'conduct.'"[63] Further, the court found that any difference between education and promotion regarding pharmaceutical marketing activities reflects "the line between pure speech and commercial speech," not a distinction between speech and conduct.[64]

After also rejecting the FDA's second argument—that "a certain subset of speech may be considered completely outside of the First Amendment framework because the speech occurs in an area of extensive government regulation"[65]—Judge Lamberth moved to the pivotal question of whether this activity amounted to pure or commercial speech. While commercial speech is typically "authored and/or uttered directly by the commercial entity that wishes to financially benefit from the message," in this case "the speech that the manufacturers wish[ed] to 'communicate' [was] the speech of others—the work product of scientists, physicians and other academics."[66] In other words, the underlying materials that the drug companies wished to distribute were unquestionably core First Amendment speech.[67] Thus, the question became whether "speech that would be fully protected as scientific and/or educational speech become[s] transformed into commercial speech, with its reduced level of protection, by the mere

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60 *Id.*

61 *Id.*

62 *Id.*

63 *Id.*

64 *Id.*

65 *Id.* at 60–62 ("Since the *Central Hudson* decision, the Supreme Court has consistently applied a speech analysis whether under the pure speech or commercial speech framework to cases involving statutes and/or regulations in areas subject to extensive state or federal regulation.").

66 *Id.* at 62.

67 *See id.*

fact that a commercial entity seeks to distribute it in order to increase its sales of the product addressed in the speech."[68]

To answer this question, the court cited *Bolger v. Youngs Drug Products Corporation*[69] for the proposition that whether a communication is commercial speech "is predicated upon the 'commonsense' distinction between speech proposing a commercial transaction . . . and other varieties of speech."[70] Following *Bolger*, the court pointed to three factors that should be considered: "(1) whether the speech is concededly an advertisement; (2) whether the speech refers to a specific product; and (3) whether the speaker has an economic motivation for disseminating the speech."[71] When all three factors are present, the communication amounts to commercial speech.[72]

Applying this test, the court held that off-label marketing is, indeed, commercial speech.[73] First, marketing materials undoubtedly fit within the definition of an advertisement, which is something that "'call[s] public attention to, especially by emphasizing desirable qualities so as to arouse a desire to buy or patronize.'"[74] Second, the materials in question referred to a specific product, namely the drug whose off-label uses the company wished to tout.[75] Finally, the drug makers conceded that they had a financial motivation for distributing the information.[76]

Having held that marketing information amounts to commercial speech, the court then applied the four-prong test announced in *Central Hudson Gas & Electric Corp. v. Public Service Commission*[77] to determine whether the prohibition could withstand constitutional scrutiny.[78] That test "directs the reviewing court to inquire whether: 1) the speech concerns lawful activity and is not misleading; 2) the asserted government interest is substantial; 3) the regulation directly advances the governmental interest asserted; and 4) the regulation is not more extensive than necessary to serve that interest."[79]

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68 *Id.* at 64.

69 Bolger v. Youngs Drug Prods. Corp., 463 U.S. 60 (1983).

70 *Friedman*, 13 F. Supp. 2d at 64 (citing *Bolger*, 463 U.S. at 64) (internal quotations omitted).

71 *Id.* (citing *Bolger*, 463 U.S. at 66).

72 *See id.*

73 *See id.*

74 *Id.* (quoting WEBSTER'S NINTH NEW COLLEGIATE DICTIONARY (1990)).

75 *See id.*

76 *See id.*

77 Cent. Hudson Gas & Elec. Corp. v. Pub. Serv. Comm'n, 447 U.S. 557 (1980).

78 *See Friedman*, 13 F. Supp. 2d at 65.

79 Hall & Sobotka, *supra* note 20, at 15 (citing Cent. Hudson, 447 U.S. at 566).

The first prong considers whether the speech concerns unlawful activities or is inherently misleading.[80] The court dismissed as tautological the FDA's argument that because promoting off-label uses is misbranding and misbranding is illegal, then promoting off-label uses must be illegal.[81] Rather, the court found the "proper inquiry is not whether the speech violates a law or regulation, but . . . whether the conduct that the speech promotes violates the law."[82] Because off-label prescription was not proscribed by law, the court answered this inquiry in the negative.[83] Further, to be "inherently misleading," the speech at issue must be "more likely to deceive the public than to inform it."[84] The court held that this was not the case because the conclusions reached by a laboratory scientist or university academic and presented in a peer-reviewed journal or textbook, or the findings presented by a physician at a CME seminar are not 'untruthful' or 'inherently misleading' merely because the FDA has not yet had the opportunity to evaluate the claim.[85]

The second question under *Central Hudson* is whether the government's asserted interest is substantial.[86] In *Friedman*, the court observed that "[t]he Supreme Court has consistently held that the government has a substantial interest in protecting the health and safety of its citizens."[87] More specifically, the court agreed with the FDA that it had a substantial interest in "provid[ing] an incentive for manufacturers to go through the strict FDA preclinical and clinical trial process to get off-label uses on-label."[88] WLF's response to the FDA's claim amounted simply to an argument "that requiring manufacturers to get new uses on-label does not, on balance, promote public health."[89] But the court rejected this argument, finding it merely questioned whether the prohibition was a wise policy—a question that was for Congress, and not the court, to decide.[90]

Third, "[u]nder the *Central Hudson* test, commercial speech restrictions must advance the government's interest in 'a direct and ma-

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80 *See Friedman*, 13 F. Supp. 2d at 65–66.

81 *See id.* at 66.

82 *Id.*

83 *See id.*

84 Cent. Hudson Gas & Elec. Corp. v. Pub. Serv. Comm'n, 447 U.S. 557, 563 (1980).

85 *Friedman*, 13 F. Supp. 2d at 67.

86 *See id.* at 69.

87 *Id.*

88 *Id.* at 70.

89 *Id.* at 71.

90 *Id.*

terial way.'"[91] "[M]ere speculation or conjecture" is not enough.[92] Rather, the government must "demonstrate that the harms it recites are real and that its restriction will in fact alleviate them to a material degree."[93] Finding that "one of the few mechanisms available to [sic] FDA to compel manufacturer behavior is to constrain their marketing options," the court held that the regulation directly advanced the government's proffered interest.[94]

Finally, under the last prong of the *Central Hudson* test, the government must have made an effort "to reasonably fit its means to its end sought."[95] The regulation does not have to be the "single best disposition, but one whose scope is in proportion to the interest served."[96] On the basis of this requirement, Judge Lamberth held the FDA's prohibition unconstitutional.[97] The court based this determination "in large part upon the fact that there exist less-burdensome alternatives to this restriction on commercial speech"—most obviously, "full, complete, and unambiguous disclosure by the manufacturer."[98]

To sum up, *Friedman* held that the marketing of a drug's off-label uses by a manufacturer constituted commercial speech and that the FDA's prohibition on that speech was unconstitutional. One caveat to the decision, however, was that drug companies still could not produce or distribute "any internally-produced marketing materials to physicians concerning off-label uses," or be involved "with seminars not conducted by an 'independent program provider.'"[99]

Although *Friedman* provides the most thorough discussion of the issues involved, Judge Lamberth's opinion is not controlling law. On appeal, the D.C. Circuit vacated the holding in *Friedman* upon deciding that there was no case or controversy, leaving the issues posed in the case unsettled.[100] The D.C. Circuit's decision was based on the FDA's clarification at oral argument that violations of the off-label marketing policy would not independently constitute misbranding.[101] Instead, the FDA maintained it would merely retain the right to use

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91 *Id.*

92 Edenfield v. Fane, 507 U.S. 761, 770–71 (1993).

93 *Id.*

94 *Friedman*, 13 F. Supp. 2d at 72.

95 *Id.*

96 Bd. of Trs. of the State Univ. of N.Y. v. Fox, 492 U.S. 469, 480 (1989) (internal quotations omitted).

97 *See Friedman*, 13 F. Supp. 2d at 72–73.

98 *Id.* at 73.

99 *Id.*

100 Wash. Legal Found. v. Henney, 202 F.3d 331, 336–37 (D.C. Cir. 2000).

101 *See id.* at 335–36.

violations as "*evidence* in a misbranding or 'intended use' enforcement action . . . ."[102] In response to the government's refined position, WLF agreed that it no longer had a constitutional objection,[103] and as a result the D.C. Circuit did not address the merits of the district court's opinion.[104]

On remand, the district court held that the original injunction was solely based on constitutional law, and so, after the D.C. Circuit's decision, there was no basis left for enjoining the agency's actions.[105] As to where that leaves the constitutionality of the FDA's regulation, one observer has written that "[m]ost likely, the battle has only begun, since the [D.C. Circuit did] acknowledge[ ] the FDA's ability to institute misbranding actions against manufacturers and the potential for First Amendment violations within this context."[106]

IV. The FDA's Regulation Is Constitutional and Sound Policy

This Part argues that even if the FDA had not "clarified" its position before the D.C. Circuit, the policy would have been constitutional. In large part, Judge Lamberth was correct in his analysis of the constitutional issues. This Essay does not disagree with the court's determination that the marketing activity amounted to commercial speech, that the *Central Hudson* test applied, that the promotional materials were not inherently misleading, or that the government had a substantial interest. The point of disagreement is with the court's analysis of the last prong of the test—whether the regulation limits more speech than necessary.

The regulation at issue here is distinguishable from the one struck down in *Thompson v. Western States Medical Center*,[107] in which the Court refined and applied the *Central Hudson* test.[108] In *Western States*, the Court held that an FDA restriction on the advertisement of compounded drugs[109] violated the First Amendment because the gov-

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102 *Id.* at 336.

103 *See id.*

104 *See id.* at 337 n.7.

105 *See* Wash. Legal Found. v. Henney, 128 F. Supp. 2d 11, 15 (D.D.C. 2000).

106 Nicole Endejann, Comment, *Is the FDA's Nose Growing?: The FDA Does Not "Exaggerate[ ] Its Overall Place in the Universe" When Regulating Speech Incident to "Off-Label" Prescription Drug Labeling and Advertising*, 35 AKRON L. REV. 491, 510 (2002).

107 Thompson v. W. States Med. Ctr., 535 U.S. 357 (2002).

108 *See id.* at 368–74.

109 "Drug compounding is a process by which a pharmacist or doctor combines, mixes, or alters ingredients to create a medication tailored to the needs of an individual patient," and is "typically used to prepare medications that are not commercially available, such as medication for a patient who is allergic to an ingredient in a mass-produced product." *Id.* at 360–61.

ernment had "failed to demonstrate that the speech restrictions [were] not more extensive than [ ] necessary" to serve its purposes.[110] The problem for the FDA in *Western States* was that it regulated advertising merely because it served as "a fair proxy" for whether a party would be a small- or large-scale manufacturer.[111] Because the government could have taken a more direct approach and regulated the manufacturing process, the Court found that the FDA's advertising prohibition restricted speech unnecessarily.[112]

Off-label prescription and use is much different, though, than what the Court encountered in *Western States*. Although compounding is necessary for many individual patients with particular needs,[113] off-label prescription and use is integral to the entire practice of medicine.[114] As the Court noted, the FDA could, for example, have "ban[ned] the use of commercial scale manufacturing or testing equipment for compounding drug products."[115] Here, the government does not seek to limit the practice of off-label prescriptions. Rather, the regulation aims to both limit the dissemination of potentially harmful materials and encourage drug companies to make current off-label uses on-label ones.[116] As acknowledged in Judge Lamberth's opinion, this cannot be done without *some* restriction of companies' speech.[117] The question then becomes whether the FDA's approach is more restrictive than necessary.

First, it must be noted that the FDA does not prohibit promotion of off-label uses in a blanket manner. Instead, for a drug company to market off-label uses, it must meet a number of requirements.[118] These include: (1) "submission of a new drug application," (2) that the material not be "abridged, false, misleading or pose[ ] a significant health risk," (3) that "any clinical research found in the information is not conducted by another manufacturer," (4) submission of "a copy of the disseminated information to the FDA," and (5) "prominently displayed disclosures with the disseminated information."[119] These re-

110 *Id.* at 371 (internal quotation omitted).

111 *See id.* at 371.

112 *See id.* at 372.

113 *See id.* at 369.

114 *See supra* note 15 and accompanying text.

115 *W. States Med. Ctr.*, 535 U.S. at 372 (internal quotation omitted).

116 *See* Wash. Legal Found. v. Friedman, 13 F. Supp. 2d 51, 70–71 (D.D.C. 1998), *vacated sub nom.* Wash. Legal Found. v. Henney, 202 F.3d 331, 337 (D.C. Cir. 2000).

117 *See id.* at 73 (advocating a full disclosure alternative to the prohibition that is "*less* restrictive on speech" (emphasis added)).

118 *See* 21 U.S.C. § 360aaa(a)–(b) (2000).

119 Endejann, *supra* note 106, at 504–05.

quirements may be an obstacle to marketing off-label uses, but they are not a complete bar.

If unrestricted off-label marketing is allowed, even with the full disclosure Judge Lamberth advocated, "three important groups—manufacturers, physicians, and scientists—all face either conflicts of interest or incentives that encourage potentially risky . . . practices."[120] Drug makers are, of course, in business to make money. If the FDA is necessary to prevent pharmaceutical companies from prematurely releasing unsafe drugs to the public, then there is no reason to believe that the companies would not be similarly "tempted to market dangerous off-label uses if permitted to do so freely."[121] As for doctors, the common practice of accepting "gratuities" from manufacturers has the potential to place the recipient "in potential positions of either blatant or subtle indebtedness, a process capable of clouding judgment in the treatment of patients."[122] This problem would only be exacerbated were the companies allowed to freely distribute materials promoting their drugs' off-label uses. Finally, scientists are susceptible to being influenced by financial ties to drug companies or, less ominously but more likely, a desire to "highlight the importance of their research."[123]

Because these concerns are present even when the participants *know* that an off-label use is suspect, they cannot be dismissed by simply requiring that drug companies disclose. Full disclosure does not alter the institutional realities. Drug companies, immunized by disclosure, will have an incentive to market more recklessly; scientists and physicians will be even more exposed to the industry's influence. Despite the allure of full disclosure's simplicity, it is not a satisfactory solution. The FDA's current policy is, on the other hand, satisfactory.

V. Conclusion

Marketing off-label drug uses unquestionably amounts to commercial speech, and thus restrictions of it must meet the *Central Hudson* requirements. Given the substantial pitfalls of unfettered off-label marketing and the fact that current regulations do not totally ban the practice, but simply condition it, Judge Lamberth's decision in *Friedman* should not be followed by future courts dealing with the issue. Even if the "full disclosure" alternative advanced in that opin-

120 Salbu, *supra* note 11, at 206.

121 *Id.*

122 *Id.* at 207.

123 *Id.* at 209.

ion restricts speech to a lesser degree,[124] it does not adequately address the FDA's main concerns. The Agency's tightly conditioned approval of off-label marketing provides a "reasonable fit" between the objectives to be served and its course of action and does not restrict speech more than necessary.

124 *See* Wash. Legal Found. v. Friedman, 13 F. Supp. 2d 51, 73 (D.D.C. 1998), *vacated sub nom.* Wash. Legal Found. v. Henney, 202 F.3d 331, 337 (D.C. Cir. 2000).